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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Marlana Titus  
Nash & Titus, LLC  
Suite 1000  
3415 Brookeville Road  
Brookeville, MD 20833

EXAMINER

CHUNDURU, SURYAPRABHA

ART UNIT

PAPER NUMBER

1637

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14

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/878,131

Applicant(s)

HONG ET AL.

Examiner

Suryaprabha Chunduru

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 26 June 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-17 is/are pending in the application.
- 4a) Of the above claim(s) 12-17 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-11 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_ 6) ☐ Other: \_\_\_\_\_

**DETAILED ACTION**

1. Applicant's election without traverse of Group I (claims 1-11) in Paper No. 13 is acknowledged.
2. The Information Disclosure Statement (Paper No. 9) filed on October 10, 2001 has been entered and considered.

***Claim Rejections - 35 USC § 112***

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

a. Claims 1-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1, 2 and 9 are indefinite because instant claims recite 'mixtures thereof' which is unclear for whether the phrase accomplishes for a mixture of glycerol and ethylene glycol or a mixture of glycerol with another solvent (for example water) or a mixture of ethylene glycol with another solvent. Amendment to clearly recite the phrase would obviate the rejection.

b. Claim 8 recites the limitation "molecules " in single primer. There is insufficient antecedent basis for this limitation in the claim. Claim 1 does not recite molecules of a primer and hence the instant claim 8 lacks antecedent basis for the said molecules.

c. Claims 9-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 9 is indefinite because instant claims recite 'molecules of a primer' which is unclear for whether the term 'molecules' accomplishes for nucleotide bases or hydrogen bonding

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molecules between template and primer. Amendment to clearly recite the term would obviate the rejection.

d. Claims 1-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1 and 9 are indefinite because instant claims recite 'below about 80<sup>0</sup> C' which is unclear for whether the actual temperature for cycle primer extension is 99<sup>0</sup> C or 70<sup>0</sup> C or 60<sup>0</sup> C or 20<sup>0</sup> C or 10<sup>0</sup> C. Amendment to clearly recite the temperature would obviate the rejection.

***Claim Rejections - 35 USC § 102***

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-8 is rejected under 35 U.S.C. 102(b) as being anticipated by Fuller (USPN. 5,432,065).

Fuller teaches a method for extending a primer or a pair of primers using an enzymatic cycle primer extension at temperatures below 80<sup>0</sup> C, wherein Fuller teaches that the method comprises (i) mixing a template DNA with a primer or a primer pair and a natural thermostable DNA polymerase selected from Bca in the presence of glycerol (10-50% v/v) or ethylene glycol (20% v/v) (see column 2, lines 3-21, and column5, lines 35-52); (i) performing repeated cycles (30 cycles) primer extension under cycle conditions fluctuating between a denaturation or melting temperature of about 60<sup>0</sup> C or below 90<sup>0</sup> C and an annealing temperature of about 45<sup>0</sup> C

or lower (see column 3, lines 17-25, column 5, lines 43-45). Further, Fuller teaches that the method comprises (i) a DNA polymerase active or stable (optimum enzymatic activity) at temperatures below 70<sup>0</sup> C (see column 2, lines 10-25); (ii) repeated cycle primer extension (see column 5, lines 43-45); amplification with forward and reverse primers may be of various lengths (see column 5, lines 35-52); cycle sequencing in the presence of ddNTPs (see column 4, lines 39-68). Thus the disclosure of Fuller meets the limitations in the instant claim.

***Claim Rejections - 35 USC § 103***

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 9-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fuller (USPN. 5,432,065) and in view of Ruano (USPN. 5,427,911).

Fuller teaches a method for extending a primer or a pair of primers using an enzymatic cycle primer extension at temperatures below 80<sup>0</sup> C, wherein Fuller teaches that the method

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comprises (i) mixing a template DNA with a primer or a primer pair and a natural thermostable DNA polymerase selected from Bca in the presence of glycerol (10-50% v/v) or ethylene glycol (20% v/v) (see column 2, lines 3-21, and column 5, lines 35-52); (i) performing repeated cycles (30 cycles) primer extension under cycle conditions fluctuating between a denaturation or melting temperature of about 60<sup>0</sup> C or below 90<sup>0</sup> C and an annealing temperature of about 45<sup>0</sup> C or lower (see column 3, lines 17-25, column 5, lines 43-45). Further, Fuller teaches that the method comprises (i) a DNA polymerase active or stable (optimum enzymatic activity) at temperatures below 70<sup>0</sup> C (see column 2, lines 10-25); (ii) repeated cycle primer extension (see column 5, lines 43-45); amplification with forward and reverse primers may be of various lengths (see column 5, lines 35-52); cycle sequencing in the presence of ddNTPs (see column 4, lines 39-68). Though Fuller teaches cycle sequencing, Fuller did not teach sequencing using amplified double-stranded reaction product without prior purification.

Ruano teaches a method for sequencing of double stranded amplified product wherein Ruano teaches that the method comprises amplification of genomic DNA and sequencing of crude amplified reaction product in the presence of labeled primer and dideoxynucleotide terminators, and performing extension reaction (see column 2, lines 3-67, column 9, lines 62-68, column 10, lines 1-60).

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made, to modify a method of DNA cycle sequencing using primer extension as taught by Fuller with a method of direct sequencing using PCR amplified product as taught by Ruano to achieve expected advantage of developing a method for enhanced sensitivity of cycle sequencing because Fuller states that "a number of useful molecular biological

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techniques capitalize on the fact that duplex DNA can be denatured under one condition and that the denatured strands can be placed at another condition wherein they can re-anneal or bind in a sequence-specific manner to synthetic primers or probes. These techniques include PCR and cycle sequencing. The key denaturation event for cycle sequencing is to separate the newly synthesized DNA strand from the template strand. Cycling in the presence of denaturation agents (glycerol) allows primer extension at low temperatures and result in accumulation of significantly more signal intensity and sequence data than that obtained without cycling (see column 2, lines 46-53, column3, lines 26-31, and column 4, lines 28-38). One alternative favoring denaturation and cycling, expressly motivated by Ruano is to use amplified duplex DNA in cycle sequencing. An ordinary practitioner would have been motivated to combine the method of Fuller with the method of Ruano in order to achieve the expected advantage of developing a sensitive method for direct sequencing of a target nucleic acid.

No claims are allowable.

### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 703-305-1004. The examiner can normally be reached on 8.30A.M. - 4.30P.M, Mon - Friday.


If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 703-308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-0294 for regular communications and - for After Final communications.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

  
Suryaprabha Chunduru

July 22, 2002

  
JEFFREY FREDMAN  
PRIMARY EXAMINER  
JEFFREY FREDMAN  
PRIMARY EXAMINER